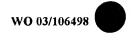


DT05 Rec'd PCT/PT0 1 3 DEC 2004 PCT/EP03/06341

SEQUENCE LISTING

<110> Crucell Holland B.V.
Bakker, Alexander B.H.
Meester-Rood, Pauline M.L.
Bakker, Adrianus Q.
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<151> 2002-06-13
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gag tgg gtc tca gct att agt ggt agt ggt agc aca tac tac gc Glu Trp Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Al 50 55 60	a 191 a
gac too gtg aag ggc cgg tto acc atc tcc aga gac aat tcc aag aa Asp Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys As 65 70 75	c 239 n
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tcc ggc gga acc ggg tct ggg act ggt acg agc gag ctc gac atc ca Ser Gly Gly Thr Gly Ser Gly Thr Gly Thr Ser Glu Leu Asp Ile Gl 130 135 140	g 431 n
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ctg atc tat ttg ggt tct aat cgg gcc tcc ggg gtc cct gac agg tt Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro Asp Arg Ph 195 200 205	c 623 e
agt ggc agt gga tca ggc aca gat ttt aca ctg aaa atc agc aga gt Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Va 210 215 220	
gag gct gag gat gtt ggg gtt tat tac tgc cag cag tac tac aac ca Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gln Gln Tyr Tyr Asn Hi 225 230 235	c 719 s
ccg acg acc ttc ggc cag ggc acc aaa ctg gaa atc aaa cgc gcg gc Pro Thr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Ala Al 240 245 250 25	a
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Trp Val Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp 50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr 65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr 85 90 95

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Gly Gly Thr Gly Ser Gly Thr Gly Thr Ser Glu Leu Asp Ile Gln Met 130 135 140

Thr Gln Ser Pro Asp Ser Leu Pro Val Thr Pro Gly Glu Pro Ala Ser 145 150 155 160

Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser Asn Gly Tyr Asn 165 170 175

Tyr Leu Asp Trp Tyr Leu Gln Lys Ala Gly Gln Ser Pro Gln Leu Leu 180 185 190

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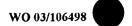
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Pro Gl	y Gly	Ser	Leu 20	Arg	Leu	Ser	Cys	Ala 25	Ala	Ser	Ğly	Phe	Thr	Phe	
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Ser Gl	y Tyr	Ser 35	Met	Asn	Trp	Val	Arg	Gln	Ala	Pro	Gly	Lys 45	Gly	Leu	143
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65				_	70	_				75	,	•	•		
aag aad Lys Asi	tca Ser	ctg	ťat Tur	ctg	caa	atg	aac	agt	ctg	aga	gcc	gag	gac	aca	287
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gcc gt	y tat	tac	tgt	gcc	aaa	gac	cgc	tac	gtc	aac	acg	tcg	aac	gcg	335
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gga ggt	tee	aac	ana	200	aaa	tot		act	aat	200	200		ot c	~ 2.0	421
Gly Gly	Ser 130	Gly	Gly	Thr	Gly	Ser	Gly	Thr	Gly	Thr	Ser	Glu	Leu	Asp	431
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	ctg Leu 240	GTĀ	ccg Pro	ccc Pro	acc Thr	ttc Phe 245	ggc Gly	cag Gln	ggc	acc Thr	aaa Lys 250	Leu	gaa Glu	atc Ile	aaa Lys	cgc Arg 255	7	67
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Gly Ser Gly Gly Thr Gly Ser Gly Thr Gly Thr Ser Glu Leu Asp Ile 130 \$135\$

Gln Met Thr Gln Ser Pro Asp Ser Leu Pro Val Thr Pro Gly Glu Pro 145 150 155 160

Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser Asn Gly
165 170 175

Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln 180 185 190

Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro Asp Arg 195 200 205

Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg 210 215 220

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Gly Pro Pro Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys Arg Ala 245 250 255

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<223>

WO 03/106498



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agc Ser	Gly	tac Tyr	cct Pro 35	atg Met	aac Asn	tgg Trp	gtc Val	cgc Arg 40	cag Gln	gcg Ala	ccc Pro	GJA	aag Lys 45	Gly	ctg Leu	143
gaģ Glu	tgg Trp	gtg Val 50	gca Ala	gtt Val	ata Ile	tca Ser	tat Tyr 55	gat Asp	gga Gly	agt Ser	aat Asn	aaa Lys 60	tac Tyr	tac Tyr	gca Ala	191
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Thr 80	Leu	Tyr	ctg Leu	Gln	Met 85	Asn	Ser	Leu	Arg	Ala 90	Glu	Asp	Thr	Ala	Val 95	287
Tyr	Tyr	Cys	gca Ala	Arg 100	Asp	Met	Ser	Gly	Phe 105	His	Glu	Phe	Asp	Tyr 110	Trp	335
Gly	Gln	Gly	acc Thr 115	Leu	Val	Thr	Val	Leu 120	Glu	Gly	Thr	Gly	Gly 125	Ser	Gly	383
Gly	Thr	Gly 130	tct Ser	Gly	Thr	Gly	Thr 135	Ser	Glu	Leu	Thr	Gln 140	Ser	Pro	Ser	431
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Val	Pro	Ser	agg Arg 195	Phe	Ser	Gly	Ser	Gly 200	Ser	Gly	Thr	Asp	Phe 205	Thr	Leu	623
Thr	Ile	Ser 210	agt Ser	Leu	Gln	Pro	Glu 215	Asp	Phe	Ala	Thr	Tyr 220	Tyr	Суз	Gln	671
Gln	Ser 225	Tyr	agt Ser	Thr	Pro	cca Pro 230	acg Thr	ttc Phe	ggc Gly	caa Gln	ggg Gly 235	acc Thr	aag Lys	gtg Val	gag Glu	719
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Gly Tyr Pro Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu 35 40 45

Trp Val Ala Val Ile Ser Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp 50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr 65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr 85 90 95

Tyr Cys Ala Arg Asp Met Ser Gly Phe His Glu Phe Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Leu Glu Gly Thr Gly Gly Ser Gly Gly 115 120 125

Thr Gly Ser Gly Thr Gly Thr Ser Glu Leu Thr Gln Ser Pro Ser Ser 130 135 140

Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr Cys Arg Ala Ser 145 150 155 160

Gln Ser Ile Ser Ser Tyr Leu Asn Trp Tyr Gln Gln Lys Pro Gly Lys 165 170 175

Ala Pro Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu Gln Ser Gly Val 180 185 190

Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr 195 200 205



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Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr Tyr Cys Gln Gln 210 215 220

Ser Tyr Ser Thr Pro Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile 225 230 235 240

Lys Arg Ala Ala

WO 03/106498

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<222> (3)..(761)

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Pro Gly Arg Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
20 25 30

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gag tgg gtc tca tcc att agt ggt ggt agc aca tac tac gca gac tcc 191 Glu Trp Val Ser Ser Ile Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser 50 55 60

agg aag ggc aga ttc acc atc tcc aga gac aat tcc aag aac acg ctg
Arg Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu
65 70 75

tat ctt caa atg aac aac ctg aga gct gag gac acg gcc gtg tat tac 287
Tyr Leu Gln Met Asn Asn Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr
80 85 90 95

tgt gca aga gac cgc tac ttc agg cag cag aac gcg ttc gat tac tgg

Cys Ala Arg Asp Arg Tyr Phe Arg Gln Gln Asn Ala Phe Asp Tyr Trp

100 105 110

ggc cag ggc acc ctg gtg acc gtg ctc gag ggt acc gga ggt tcc ggc 383 Gly Gln Gly Thr Leu Val Thr Val Leu Glu Gly Thr Gly Gly Ser Gly 115 120





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cag Gln	tct Ser 145	cca Pro	gtc Val	acc Thr	ctg Leu	ccc Pro 150	gtc Val	acc Thr	cct Pro	gga Gly	gag Glu 155	ccg Pro	gcc Ala	tcc Ser	atc Ile	479
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ttg Leu	gat Asp	tgg Trp	tac Tyr	ctg Leu 180	cag Gln	aag Lys	cca Pro	Gly ggg	cag Gln 185	tct Ser	cca Pro	cag Gln	ctc Leu	ctg Leu 190	atc Ile	575
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Trp Val Ser Ser Ile Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Arg 50 55 60

Lys Gly Arg Phe Thr lle Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr 65 70 75 80



Leu Gln Met Asn Asn Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys
85 90 95

Ala Arg Asp Arg Tyr Phe Arg Gln Gln Asn Ala Phe Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Leu Glu Gly Thr Gly Gly Ser Gly Gly 115 120 125

Thr Gly Ser Gly Thr Gly Thr Ser Glu Leu Asp Ile Gln Met Thr Gln 130 135 140

Ser Pro Val Thr Leu Pro Val Thr Pro Gly Glu Pro Ala Ser Ile Ser 145 150 155 160

Cys Arg Ser Ser Gln Ser Leu Leu His Ser Asn Gly Tyr Asn Tyr Leu 165 170 175

Asp Trp Tyr Leu Gln Lys Pro Glý Gln Ser Pro Gln Leu Leu Ile Tyr 180 185 190

Leu Gly Ser Asn Arg Ala Ser Gly Val Pro Asp Arg Phe Ser Gly Ser 195 200 205

Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu Ala Glu 210 215 220

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<222> (3)..(746)

<223>

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gat ttt acc ctg acc atc agc agc ctg cag ccg gaa gat ttc gct acc Asp Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr 210 215 220	671
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Trp Val Ala Asn Ile Asn Gln Asp Gly Asn Glu Lys Tyr Tyr Ala Asp 50 55 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Ser 65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Arg Asp Glu Asp Thr Ala Leu Tyr 85 90 95

Tyr Cys Ala Arg Ala Arg Ala Ala Gly Thr Ile Phe Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Leu Glu Gly Thr Gly Gly Ser Gly Gly
115 120 125

Thr Gly Ser Gly Thr Gly Thr Ser Glu Leu Asp Ile Gln Met Thr Gln 130 135 140

Ser Pro Ser Ser Leu Ser Ala Ser Val Gly Asp Arg Val Thr Ile Thr 145 150 150 160

Cys Arg Ala Ser Gln Asn Val Ser Asn Tyr Leu Thr Trp Tyr Gln Gln
165 170 175

Lys Pro Gly Lys Ala Gly Lys Leu Leu Ile Tyr Ala Ala Ser Ser Leu 180 185 190

Gln Ser Gly Val Pro Ser Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp 195 200 205

17

Phe Thr Leu Thr Ile Ser Ser Leu Gln Pro Glu Asp Phe Ala Thr Tyr 210 215 220

Tyr Cys Gln Gln Ser Tyr Phe Asn Pro Ala Thr Phe Gly Gln Gly Thr 225 230 235 240

Lys Leu Glu Ile Lys Arg Ala Ala 245

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<211> 769

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<223> scFv SC02021

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<221> CDS

<222> (3)..(767)

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Pro Arg Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe
20 25 30

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gag tgg gtg gca gtt ata tca tat gat gga agc aat aaa tac tac gca 191 Glu Trp Val Ala Val Ile Ser Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala

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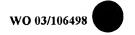
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100 105 110

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120
125



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aac tat ttg gat tgg tac ctg cag aag cca ggg cag tct cca cag ctc Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu 180 185 190	575
ctg atc tat ttg ggt tct aat cgg gcc tcc ggg gtc cct gac agg ttc Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro Asp Arg Phe 195 200 205	623
agt ggc agt gga tca ggc aca gat ttt aca ctg aaa atc agc aga gtg Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val 210 215 220	671
gag gct gag gat gtt ggg gtt tat tac tgc cag cag tac aag tcg aac Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gln Gln Tyr Lys Ser Asn 225 235	719
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Arg Gly Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser 20 25 30

Ser Tyr Ala Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu 35 40 45

Trp Val Ala Val Ile Ser Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp 50 60

Ser Val Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr 65 70 75 80

Leu Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr 85 90 95

Tyr Cys Ala Lys Asp Arg Tyr Ile Thr Leu Pro Asn Ala Leu Asp Tyr 100 105 110

Trp Gly Gln Gly Thr Leu Val Thr Val Leu Glu Gly Thr Gly Gly Ser 115 120 125

Gly Gly Thr Gly Ser Gly Thr Gly Thr Ser Glu Leu Asp Ile Gln Met 130 135 140

Thr Gln Ser Pro Val Ser Leu Pro Val Thr Pro Gly Glu Pro Ala Ser 145 150 155 160

Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser Asn Gly Tyr Asn 165 170 175

Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser Pro Gln Leu Leu 180 185 190

Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro Asp Arg Phe Ser 195 200 205

Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile Ser Arg Val Glu 210 215 220

Ala Glu Asp Val Gly Val Tyr Tyr Cys Gln Gln Tyr Lys Ser Asn Pro 225 230 235 240

Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys Arg Ala Ala 245 250 255

<210> 13

<211> 745

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cct	ggg Gly	ggg	tcc Ser	ctg Leu	5 aga Arg	ctc Leu	tcc Ser	tgt Cys	gca Ala	ggc Gly	tct Ser	gga Gly	ttc Phe	Thr	ttc Phe	95
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gag Glu	tgg Trp	gta Val 50	tca	gct Ala	att Ile	ggt Gly	acc Thr 55	ggt	ggt Gly	ggc Gly	aca Thr	tac Tyr 60	tat	gca Ala	gac Asp	191
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ttg Leu 80	tát Tyr	ctt Leu	caa Gln	atg Met	aac Asn 85	agc Ser	ctg Leu	aga Arg	gcc Ala	gag Glu 90	gac Asp	acg Thr	gcc Ala	gtg Val	tat Tyr 95	287
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tgg Trp	ggc Gly	caa Gln	gġt Gly 115	acc Thr	ctg Leu	gtc Val	acc Thr	gtc Val 120	tcg Ser	agt Ser	ggt Gly	gga Gly	ggc Gly 125	ggt Gly	tca Ser	383
ggc Gly	gga Gly	ggt Gly 130	ggc Gly	tct Ser	ggc Gly	ggt Gly	ggc Gly 135	gga Gly	tcg Ser	gaa Glu	att Ile	gag Glu 140	ctc Leu	aca Thr	cag Gln	431
tct Ser	cca Pro 145	gcc Ala	acc Thr	ctg Leu	tct Ser	ttg Leu 150	tct Ser	cca Pro	Gly ggg	gaa Glu	aga Arg 155	gcc Ala	acc Thr	ctc Leu	tcc Ser	479
tgc Cys 160	agg Arg	gcc Ala	agt Ser	cag Gln	agt Ser 165	gtt Val	agc Ser	agc Ser	tac Tyr	tta Leu 170	gcc Ala	tgg Trp	tac Tyr	caa Gln	cag Gln 175	527
aaa Lys	cct Pro	ggc Gly	cag Gln	gct Ala 180	ccc Pro	agg Arg	ctc Leu	ctc Leu	atc Ile 185	tat Tyr	gat Asp	gca Ala	tcc Ser	aac Asn 190	agg Arg	575
Ala	Thr	ggc Gly	11e 195	Pro	Ala	Arg	Phe	Ser 200	Gly	Ser	Gly	Ser	Gly 205	Thr	Asp	623
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tac Tyr	tgt Cys 225	cag Gln	cag Gln	cgt Arg	agc Ser	aac Asn 230	tgg Trp	cct Pro	ccg Pro	gct Ala	ttc Phe 235	ggc Gly	gga Gly	G1A aaa	acc Thr	719
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<212> PRT

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Gly Gly Ser Leu Arg Leu Ser Cys Ala Gly Ser Gly Phe Thr Phe Ser 20 25 30

Ser Tyr Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu 35 40 45

Trp Val Ser Ala Ile Gly Thr Gly Gly Gly Thr Tyr Tyr Ala Asp Ser 50 55 60

Val Gln Gly Arg Phe Thr Ile Ser Arg Asp Asn Ala Lys Asn Ser Leu 65 70 75 80

Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr 85 90 95

Cys Ala Arg Tyr Asp Glu Pro Leu Thr Ile Tyr Trp Phe Asp Ser Trp
100 105 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Gly Ser Gly 115 120 125

Gly Gly Gly Ser Gly Gly Gly Ser Glu Ile Glu Leu Thr Gln Ser 130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys 145 150 150 160

Arg Ala Ser Gln Ser Val Ser Ser Tyr Leu Ala Trp Tyr Gln Gln Lys 165 170 175

Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Asp Ala Ser Asn Arg Ala 180 185 190

Thr Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe 195 200 205 Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr 210 215 220

Cys Gln Gln Arg Ser Asn Trp Pro Pro Ala Phe Gly Gly Gly Thr Lys 225 230 235 240

Val Glu Ile Lys Arg Ala Ala

<210> 15

<211> 745

<212> DNA

<213> Artificial sequence

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<223> scFv SC02023

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<221> CDS

<222> (3)..(743)

<223>

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20 25 30

agt agc tat gct atg cac tgg gtt cgc cag gct cca gga aaa ggt ctg

143

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35

40

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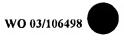
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Ser Val Met Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr
65

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tac tgt gca aga tac gac aat gtg atg ggt ctt tac tgg ttt gac tac
Tyr Cys Ala Arg Tyr Asp Asn Val Met Gly Leu Tyr Trp Phe Asp Tyr
100 105 110

tgg ggc caa ggt acc ctg gtc acc gtc tcg agt ggt gga ggc ggt tca 383





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tct Ser	cca Pro 145	gcc Ala	acc Thr	ctg Leu	tct Ser	ttg Leu 150	tct Ser	cca Pro	ggg Gly	gaa Glu	aga Arg 155	gcc Ala	acc Thr	ctc Leu	tcc Ser	479
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Trp Val Ser Ala Ile Gly Thr Gly Gly Gly Thr Tyr Tyr Ala Asp Ser 50 60

Val Met Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu 65 70 75 80

Tyr Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr 85 90 95

Cys Ala Arg Tyr Asp Asn Val Met Gly Leu Tyr Trp Phe Asp Tyr Trp 100 105 110

Gly Gln Gly Thr Leu Val Thr Val Ser Ser Gly Gly Gly Ser Gly 115 120 125

Gly Gly Gly Ser Gly Gly Gly Gly Ser Glu Ile Glu Leu Thr Gln Ser 130 135 140

Pro Ala Thr Leu Ser Leu Ser Pro Gly Glu Arg Ala Thr Leu Ser Cys 145 150 155 160

Arg Ala Ser Gin Ser Val Ser Ser Tyr Leu Ala Trp Tyr Gln Gln Lys 165 170 175

Pro Gly Gln Ala Pro Arg Leu Leu Ile Tyr Asp Ala Ser Asn Arg Ala 180 185 190

Thr Gly Ile Pro Ala Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe 195 200 205

Thr Leu Thr Ile Ser Ser Leu Glu Pro Glu Asp Phe Ala Val Tyr Tyr 210 215 220

Cys Gln Gln Arg Ser Asn Trp Pro Pro Ala Phe Gly Gly Gly Thr Lys 225 230 235 240

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<211> 12

<212> PRT

<213> Artificial sequence

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<223> CDR3 of scFv SC02008

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<211> 12

<212> PRT

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<223> CDR3 of scFv SC02009

<400> 18

Asp Arg Tyr Val Asn Thr Ser Asn Ala Phe Asp Tyr 1 5 10

<210> 19

<211> 10

<212> PRT

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Asp Met Ser Gly Phe His Glu Phe Asp Tyr 1 5 10

<210> 20

<211> 12

<212> PRT

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<223> CDR3 of scFv SC02011

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<210> 21

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<212> PRT

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<223> CDR3 of scFv SC02012

<400> 21

Ala Arg Ala Ala Gly Thr Ile Phe Asp Tyr 1 5 10

<210> 22

<211> 12

<212> PRT

<213> Artificial sequence

<220>

<223> CDR3 of scFv SC02021

<400> 22

Asp Arg Tyr Ile Thr Leu Pro Asn Ala Leu Asp Tyr 1 5 10

<210> 23

<211> 12

<212> PRT

<213> Artificial sequence

<220>

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<400> 23

Tyr Asp Glu Pro Leu Thr Ile Tyr Trp Phe Asp Ser 1 5 10

<210> 24

<211> 12

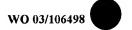
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<400> 24



Tyr Asp Asn Val Met Gly Leu Tyr Trp Phe Asp Tyr 1 5 10

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<211> 451

<212> PRT

<213> Artificial sequence

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<223> Amino acid sequence of heavy chain of 008

<400> 25

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Thr Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val 35 40 45

Ser Ala Ile Ser Gly Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Val 50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr 65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys 85 90 95

Ala Lys Asp Arg Tyr Ser Gln Val His Tyr Ala Leu Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser 115 120 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala 130 135 140

Äla Leu Gly Cys Leu Vál Lys Asp Tyr Phe Pro Glu Pro Val Thr Val 145 150 155 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala 165 170 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val
180 185 190



Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His 195 200 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys 210 215 220

Asp Lýs Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly 225 230 235 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met 245 250 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His 260 265 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val 275 280 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr 290 295 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly 315 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile 325 330 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val 340 345 350

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser 355 360 365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu 370 375 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro 385 390 395 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val 405 410 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met 420 425 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser 435 440 445

Pro Gly Lys 450 <210> 26

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<212> PRT

<213> Artificial sequence

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<223> Amino acid sequence of heavy chain of 011

<400> 26

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1 5 10 15

Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Asp Tyr 20 25 30

Thr Met Asn Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val 35 40 45

Ser Ser Ile Ser Gly Gly Ser Thr Tyr Tyr Ala Asp Ser Arg Lys Gly 50 55 60

Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu Gln 65 70 75 80

Met Asn Asn Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala Arg 85 90 95

Asp Arg Tyr Phe Arg Gln Gln Asn Ala Phe Asp Tyr Trp Gly Gln Gly 100 105 110

Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val Phe 115 120 125

Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala Leu 130 135 140

Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser Trp 145 150 155 160

Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val Leu 165 170 175

Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro Ser 180 185 190

Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His Lys Pro 195 200 205 Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp Lys 210 215 220

Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly Pro 225 230 235 240

Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile Ser 245 250 255

Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu Asp 260 265 270

Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His Asn 275 280 285

Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg Val 290 295 300

Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys Glu 305 310 315 320

Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu Lys 325 330 335

Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr Thr 340 345 350

Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu Thr 355 360 365

Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp Glu 370 375 380

Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val Leu 385 390 395 400

Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp Lys 405 410 415

Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met His Glu 420 425 430

Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro Gly
435 440 445

Lys

<210> 27

<211> 451

<212> PRT

<213> Artificial sequence

<220>

<223> Amino acid sequence of heavy chain 021

<400> 27

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Ser Leu Arg Leu Ser Cys Ala Ala Ser Gly Phe Thr Phe Ser Ser Tyr 20 25 30

Ala Met Asn Trp Val Arg Gln Ala Fro Gly Lys Gly Leu Glu Trp Val 35 40 45

Ala Val Ile Ser Tyr Asp Gly Ser Asn Lys Tyr Tyr Ala Asp Ser Val 50 55 60

Lys Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr 65 70 75 80

Leu Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys 85 90 95

Ala Lys Asp Arg Tyr Ile Thr Leu Pro Asn Ala Leu Asp Tyr Trp Gly
100 105 110

Gln Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser 115 120 125

Val Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala 130 135 140

Ala Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val 145 150 155 160

Ser Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala 165 170 175

Val Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val 180 185 190

Pro Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Asn Val Asn His 195 200 205

Lys Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys 210 215 220



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Asp Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly 225 230 235 240

Gly Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met 245 250 255

Ile Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His 260 265 270

Glu Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val 275 280 285

His Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr 290 295 300

Arg Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly 305 310 315 320

Lys Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile 325 330 335

Glu Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val 340 345 350

Tyr Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser 355 360 365

Leu Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu 370 375 380

Trp Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro 385 390 395 400

Val Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val 405 410 415

Asp Lys Ser Arg Trp Gln Gln Gly Asn Val Phe Ser Cys Ser Val Met 420 425 430

His Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser 435 440 445

Pro Gly Lys 450

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<212> PRT

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<223> Amino acid sequence of heavy chain of 023

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Ala Met His Trp Val Arg Gln Ala Pro Gly Lys Gly Leu Glu Trp Val
35 40 45

Ser Ala Ile Gly Thr Gly Gly Gly Thr Tyr Tyr Ala Asp Ser Val Met 50 55 60

Gly Arg Phe Thr Ile Ser Arg Asp Asn Ser Lys Asn Thr Leu Tyr Leu 65 70 75 80

Gln Met Asn Ser Leu Arg Ala Glu Asp Thr Ala Val Tyr Tyr Cys Ala 85 90 95

Arg Tyr Asp Asn Val Met Gly Leu Tyr Trp Phe Asp Tyr Trp Gly Gln 100 105 110

Gly Thr Leu Val Thr Val Ser Ser Ala Ser Thr Lys Gly Pro Ser Val 115 120 125

Phe Pro Leu Ala Pro Ser Ser Lys Ser Thr Ser Gly Gly Thr Ala Ala 130 135 140

Leu Gly Cys Leu Val Lys Asp Tyr Phe Pro Glu Pro Val Thr Val Ser 145 150 155 160

Trp Asn Ser Gly Ala Leu Thr Ser Gly Val His Thr Phe Pro Ala Val 165 . 170 175

Leu Gln Ser Ser Gly Leu Tyr Ser Leu Ser Ser Val Val Thr Val Pro 180 185 190

Ser Ser Ser Leu Gly Thr Gln Thr Tyr Ile Cys Ash Val Asn His Lys 195 200 205

Pro Ser Asn Thr Lys Val Asp Lys Arg Val Glu Pro Lys Ser Cys Asp 210 215 220

Lys Thr His Thr Cys Pro Pro Cys Pro Ala Pro Glu Leu Leu Gly Gly 225 230 235 240



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Pro Ser Val Phe Leu Phe Pro Pro Lys Pro Lys Asp Thr Leu Met Ile 245 250 255

Ser Arg Thr Pro Glu Val Thr Cys Val Val Val Asp Val Ser His Glu 260 265 270

Asp Pro Glu Val Lys Phe Asn Trp Tyr Val Asp Gly Val Glu Val His 275 280 285

Asn Ala Lys Thr Lys Pro Arg Glu Glu Gln Tyr Asn Ser Thr Tyr Arg 290 295 300

Val Val Ser Val Leu Thr Val Leu His Gln Asp Trp Leu Asn Gly Lys 305 310 315 320

Glu Tyr Lys Cys Lys Val Ser Asn Lys Ala Leu Pro Ala Pro Ile Glu 325 330 335

Lys Thr Ile Ser Lys Ala Lys Gly Gln Pro Arg Glu Pro Gln Val Tyr 340 345 350

Thr Leu Pro Pro Ser Arg Glu Glu Met Thr Lys Asn Gln Val Ser Leu 355 360 365

Thr Cys Leu Val Lys Gly Phe Tyr Pro Ser Asp Ile Ala Val Glu Trp 370 375 380

Glu Ser Asn Gly Gln Pro Glu Asn Asn Tyr Lys Thr Thr Pro Pro Val 385 390 395 400

Leu Asp Ser Asp Gly Ser Phe Phe Leu Tyr Ser Lys Leu Thr Val Asp 405 410 415

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Glu Ala Leu His Asn His Tyr Thr Gln Lys Ser Leu Ser Leu Ser Pro 435 440 445

Gly Lys 450

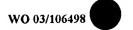
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<223> Amino acid sequence of light chain of 008

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Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Ala Gly Gln Ser 35 40 45

Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro 50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile 65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gln Gln Tyr 85 90 95

Tyr Asn His Pro Thr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys 100 105 110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu 115 120 125

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe 130 135 140

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln 145 150 150 160

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser 165 170 175

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu 180 185 190

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser 195 200 205

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys 210 215

<210> 30

<211> 219

<212> PRT

<213> Artificial sequence

<220>

<223> Amino acid sequence of light chain of 011

<400> 30

Asp Ile Val Met Thr Gln Ser Pro Asp Ser Leu Pro Val Thr Pro Gly
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Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser 20 25 30

Asn Gly Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Ala Gly Gln Ser 35 40 45

Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro 50 55 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile 65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gln Gln Tyr 85 90 95

Tyr Asn His Pro Thr Thr Phe Gly Gln Gly Thr Lys Leu Glu Ile Lys
100 105 110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu 115 120 125

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe 130 135 140

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln 145 150 150 160

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser 165 170 175

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu 180 185 190

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser 195 200 205

Pro Val Thr Lys Ser Phe Asn Arg Gly Glu Cys 210 215

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<211> 219

<212> PRT

<213> Artificial sequence

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<223> Amino acid sequence of light chain of 021

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Asp Ile Gln Met Thr Gln Ser Pro Val Ser Leu Pro Val Thr Pro Gly
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Glu Pro Ala Ser Ile Ser Cys Arg Ser Ser Gln Ser Leu Leu His Ser 20 25 30

Asn Glý Tyr Asn Tyr Leu Asp Trp Tyr Leu Gln Lys Pro Gly Gln Ser 35 40 45

Pro Gln Leu Leu Ile Tyr Leu Gly Ser Asn Arg Ala Ser Gly Val Pro 50 60

Asp Arg Phe Ser Gly Ser Gly Ser Gly Thr Asp Phe Thr Leu Lys Ile 65 70 75 80

Ser Arg Val Glu Ala Glu Asp Val Gly Val Tyr Tyr Cys Gln Gln Tyr 85 90 95

Lys Ser Asn Pro Pro Thr Phe Gly Gln Gly Thr Lys Val Glu Ile Lys
100 105 110

Arg Thr Val Ala Ala Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu 115 120 125

Gln Leu Lys Ser Gly Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe 130 135 140

Tyr Pro Arg Glu Ala Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln 145 150 150 160

Ser Gly Asn Ser Gln Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser 165 170 175

Thr Tyr Ser Leu Ser Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu 180 185 190

Lys His Lys Val Tyr Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser

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<223> Amino acid sequence of light chain of 023

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Leu Ala Trp Tyr Gln Gln Lys Pro Gly Gln Ala Pro Arg Leu Leu Ile 35 40 45

Tyr Asp Ala Ser Asn Arg Ala Thr Gly Ile Pro Ala Arg Phe Ser Gly 50 60

Ser Gly Ser Gly Thr Asp Phe Thr Leu Thr Ile Ser Ser Leu Glu Pro 65 70 75 80

Glu Asp Phe Ala Val Tyr Tyr Cys Gln Gln Arg Ser Asn Trp Pro Pro 85 90 95

Ala Phe Gly Gly Gly Thr Lys Val Glu Ile Lys Arg Thr Val Ala Ala 100 105 110

Pro Ser Val Phe Ile Phe Pro Pro Ser Asp Glu Gln Leu Lys Ser Gly 115 120 125

Thr Ala Ser Val Val Cys Leu Leu Asn Asn Phe Tyr Pro Arg Glu Ala 130 135 140

Lys Val Gln Trp Lys Val Asp Asn Ala Leu Gln Ser Gly Asn Ser Gln 145 150 150 160

Glu Ser Val Thr Glu Gln Asp Ser Lys Asp Ser Thr Tyr Ser Leu Ser 165 170 175

Ser Thr Leu Thr Leu Ser Lys Ala Asp Tyr Glu Lys His Lys Val Tyr 180 185 190

Ala Cys Glu Val Thr His Gln Gly Leu Ser Ser Pro Val Thr Lys Ser 195 200 205 Phe Asn Arg Gly Glu Cys 210

<210> 33

<211> 55

<212> DNA

<213> Artificial sequence

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<223> 5' cloning site of pPicZalphaB

<220>

<221> CDS

<222> (1)..(54)

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<400> 33

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ccg gcc g 55
Pro Ala

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<212> PRT

<213> Artificial sequence

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<223> 5' cloning site of pPicZalphaB

<400> 34

Pro Ala

<210> 35

<211> 55

<212> DNA



<213> Artificial sequence

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<223> 5' cloning site of pPicZFVH

<220>

<221> CDS

<222> (1)..(54)

<223>

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Ser Leu Glu Lys Arg Ala Met Glu Ala Ala Gly Ile His Val Ala Gln
1 5 10 15

ccg gcc g Pro Ala

<210> 36

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<213> Artificial sequence

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<223> 5' cloning site of pPicZFVH

<400> 36

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Pro Ala

<210> 37

<211> 92

<212> DNA

<213> Artificial sequence

<220>

<223> Synthetic hinge region

<220>

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<221> CDS

<222> (1)..(90)

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Cys Pro Gly Ser Gly Gly Ala Pro Ile Asp Ser Gly Phe Leu
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<210> 38

<211> 30

<212> PRT

<213> Artificial sequence

<220>

<223> Synthetic hinge region

<400> 38

Ala Ala Ala Pro Lys Pro Ser Thr Pro Pro Gly Ser Ser Cys Pro Pro 1 5 10 15

Cys Pro Gly Ser Gly Gly Ala Pro Ile Asp Ser Gly Phe Leu 20 25 30

<210> 39

<211> 1416

<212> DNA

<213> Artificial sequence

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<223> Nucleotide sequence of heavy chain of 008

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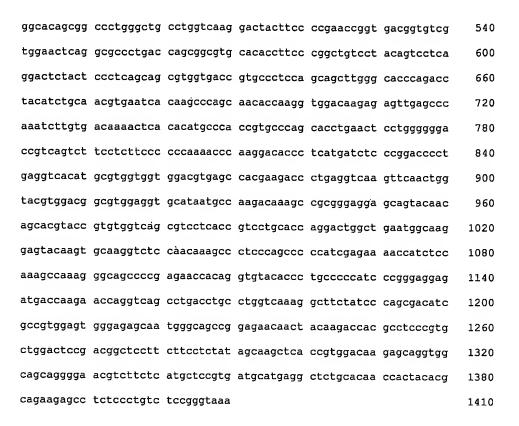
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<213> Artificial sequence

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<223> Nucleotide sequence of heavy chain of 011

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<210> 41

<211> 1416

<212> DNA

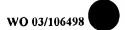
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<220>

<223> Nucleotide sequence of heavy chain of 021

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<212> DNA

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<213> Artificial sequence

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<211> 720

<212> DNA

<213> Artificial sequence

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<223> Nucleotide sequence of light chain of 011

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<211> 720

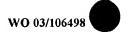
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<213> Artificial sequence

<220>

<223> Nucleotide sequence of light chain of 021

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